



The influence of pregnancy termination on the outcome of subsequent pregnancies: retrospective cohort study

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2013-002803
Article Type:	Research
Date Submitted by the Author:	27-Feb-2013
Complete List of Authors:	Scholten, Brenda; University Medical Center Utrecht, Obstetrics Page-Christiaens, Godelieve; University Medical Center Utrecht, Obstetrics Franx, Arie; University Medical Center Utrecht, Obstetrics Hukkelhoven, Chantal; Netherlands Perinatal Registry, Koster, Maria; University Medical Center Utrecht, Obstetrics
Primary Subject Heading:	Obstetrics and gynaecology
Secondary Subject Heading:	Obstetrics and gynaecology
Keywords:	termination of pregnancy, preterm delivery, cervical incompetence, placenta praevia, placental abruption, retained placenta

SCHOLARONE™
Manuscripts

Title page

The influence of pregnancy termination on the outcome of subsequent pregnancies: retrospective cohort study	Title
Brenda L Scholten, Godelieve C M L Page-Christiaens, Arie Franx, Chantal W P M Hukkelhoven, Maria P H Koster	Author's name
University Medical Center Utrecht, Lundlaan 6, 3584 EA, Utrecht, PO box 85090, 3508 AB, Utrecht, The Netherlands Brenda Scholten, MSc Department of Obstetrics, University Medical Center Utrecht, Godelieve Page-Christiaens, gynaecologist Department of Obstetrics, University Medical Center Utrecht, Arie Franx, professor of Obstetrics Netherlands Perinatal Registry, Mercatorlaan 1200, Room 46 PO box8588, 3503 RN, Utrecht, The Netherlands, Chantal Hukkelhoven, epidemiologist Department of Obstetrics, University Medical Center Utrecht, Maria Koster, epidemiologist	Address for each author
Godelieve Page-Christiaens, University Medical Center Utrecht, Lundlaan 6, Room KE 04.123.1, PO box 85090, 3508 AB Utrecht, The Netherlands, L.Christiaens@umcutrecht.nl Tel +31 88 755 6426, Fax +31 88 755 5320	Corresponding author
Termination of pregnancy, cervical incompetence, preterm delivery, placenta implantation and retention problems	Keywords
1.870	Word count

Abstract

Objective: To compare the incidences of preterm delivery, cervical incompetence treated by cerclage, placenta implantation or retention problems (i.e. placenta praevia, placental abruption and retained placenta) and postpartum haemorrhage between women with and without a history of pregnancy termination.

Design: Retrospective cohort study using aggregated data from a national perinatal registry.

Setting: All midwifery practices and hospitals in the Netherlands.

Participants: All pregnant women with a singleton pregnancy without congenital malformations and a gestational age of ≥ 20 weeks who delivered between January 2000 and December 2007.

Main outcome measures: Preterm delivery, cervical incompetence treated by cerclage, placenta praevia, placental abruption, retained placenta and postpartum haemorrhage

Results: A previous pregnancy termination was reported in 16.000 (1.2%) deliveries. The incidence of all outcome measures was significantly higher in women with a history of pregnancy termination. Adjusted odds ratios (95% confidence interval) for cervical incompetence treated by cerclage, preterm delivery, placenta implantation or retention problems and postpartum haemorrhage were 4.6 (2.9-7.2), 1.11 (1.02-1.20), 1.42 (1.29-1.55) and 1.16 (1.08-1.25), respectively. Associated numbers needed to harm were 1000, 167, 111 and 111, respectively. For any listed adverse outcome the number needed to harm was 63.

Conclusions: In this large nationwide cohort study termination of pregnancy was associated with an increased risk for preterm delivery, cervical incompetence treated by cerclage, placenta implantation or retention problems and postpartum haemorrhage in a subsequent pregnancy. Absolute risks for these outcomes however remain small.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Article Summary

Article focus

- To estimate the influence of pregnancy termination on the outcome of subsequent pregnancies.
- Does termination of pregnancy lead to cervical incompetence and/or preterm delivery in subsequent pregnancies?
- Is termination of pregnancy associated with a higher risk of placenta implantation or retention problems (i.e. placenta praevia, placental abruption and retained placenta) in a subsequent pregnancy?

Key Messages

- A termination of pregnancy is associated with an increased risk for preterm delivery, cervical incompetence treated by cerclage, placenta implantation/retention problems and postpartum hemorrhage in a subsequent singleton pregnancy.

Strengths and limitations of this study

- Largest cohort study on reproductive outcomes of women with and without a history of pregnancy termination.
- Registration of and adjustment for many potential confounders.
- The perinatal registry contains no information on the technique of pregnancy termination.
- The number of and gestational age at pregnancy terminations in a given woman was not registered
- Underreporting of pregnancy termination leads to an underestimation of its effect on future reproduction.

INTRODUCTION

Worldwide each year at least 43 million pregnancies are terminated, often in young nulliparous women.¹ Data on the effect on future pregnancies suggest an increase in risk for complications in subsequent pregnancies after pregnancy termination.²⁻¹²

In the Netherlands, approximately 32.000 pregnancies are terminated each year.¹³ The abortion rate has been unchanged since 2001 with 8.8 per thousand women of childbearing age (15 to 44 years) resident in the Netherlands having a pregnancy terminated each year.¹³ The vast majority (90-95%) of these abortions are performed in specialized clinics by surgical methods namely vacuum aspiration and curettage.¹³⁻¹⁴ In 1999, medicinal abortion with a combination of antiprogestagens and prostaglandins has been introduced in clinical practice. However, in the Netherlands this method is mainly used for termination of pregnancy for medical or genetic reasons and usually not offered as an alternative to women requesting abortion for nonmedical reasons.

The question arises how women should be counseled as to the effect of surgical abortion on future reproductive performance. We therefore set out to compare the incidences of 1) preterm delivery, 2) cervical incompetence treated by cerclage, 3) placenta implantation or retention problems (PIRP) which include placenta praevia, placental abruption and retained placenta and 4) postpartum hemorrhage (PPH) in pregnancies of women with and without a history of pregnancy termination.

METHODS

Study population

Prospectively collected data were derived from the Netherlands Perinatal Registry (PRN).¹⁵ The PRN is a Dutch nationwide database that contains demographics and information about mother and newborn, course and outcome of pregnancy, and content and organization of care. Around 96% of all deliveries from 20 weeks of gestation onwards are registered in the PRN. The database consists of three linked and validated registries: the national obstetric database for midwives (LVR-1), the national obstetric database for gynecologists (LVR-2) and the national neonatal/pediatric database (LNR).¹⁶⁻¹⁷ The study period was from January 2000 till and including December 2007. All multiple births and births of a child with a congenital anomaly in index pregnancies were excluded. Also all women where labor was induced or a planned caesarean section was performed before 37 weeks gestation, i.e. iatrogenic preterm deliveries, were excluded (*Figure 1*). Whether there had been a previous termination of pregnancy or not was registered based on responses given by the pregnant woman in a predefined pregnancy intake questionnaire, amongst others on reproductive history. This questionnaire is being filled out at the first prenatal visit, usually around 12 weeks of pregnancy. The number of pregnancy terminations in an individual woman is not

registered in the PRN. The primary study outcomes were preterm delivery, cervical incompetence with placement of a cerclage, PIRP and PPH.

Definitions

Preterm delivery was defined as delivery between 20 and 37 weeks of gestation. For a subgroup analysis of gestational age at delivery we divided gestational age into 5 groups: 20⁺⁰ to 23⁺⁶ weeks, 24⁺⁰ to 28⁺⁶ weeks, 29⁺⁰ to 32⁺⁶ weeks, 33⁺⁰ to 36⁺⁶ weeks and 37 weeks and later. In the Netherlands a cervical cerclage is considered to be indicated when there is shortening or dilatation of the cervix without contractions during the second trimester of pregnancy.^{18,19} A history of pregnancy termination is not a reason for cerclage.

Placenta praevia, placental abruption and retained placenta have been merged into the composite measure PIRP because of the low incidence of these outcomes. Retained placenta also includes postpartum curettage for incomplete placenta. PPH was defined as more than 1000 milliliters blood loss postpartum.

Prior cervical surgery includes conization or amputation of the cervix. Polyhydramnios was defined as an estimated amount of amniotic fluid of more than two liters, diagnosed by ultrasound during pregnancy. Perinatal mortality was defined as stillbirth or death up to 7 days after birth, after a gestation period of at least 22 weeks.

Socioeconomic status (SES) was based on the average income level of the neighborhood, which was determined by the first four digits of the woman's postal code, a common method for establishing SES in the Netherlands.

Statistical analysis

We used t-tests and chi-square tests to compare baseline characteristics and the difference in incidence of outcome measures between both groups. Logistic regression analysis was performed to calculate crude odds ratios (cOR) and adjusted odds ratios (aOR) and their 95% confidence intervals (95% CI). Odds ratios were adjusted for variables that are considered as possible confounders in the literature: maternal age, gravidity, parity, SES, ethnicity, smoking, drug dependence, pyelitis, polyhydramnios, current uterus myomatosis, history of preterm delivery; cervical incompetence; placenta praevia; placental abruption; manual removal of the placenta; PPH (not due perineal trauma) and cervical surgery.²⁰⁻²⁴

A subgroup analysis of various categories of gestational age was performed for the outcome preterm delivery because a deleterious effect of cervical dilatation at time of delivery could be larger at early gestational ages.

We computed a number needed to harm (1/risk difference) in which the risk difference equaled the estimated incidence in women with a history of pregnancy termination minus the

incidence among women without a history of pregnancy termination. All analyses were done using SPSS version 19.

RESULTS

During the study period 1,357,894 singletons were born who fulfilled the selection criteria (*Figure 1*). In 16,000 deliveries (1.2%) the mother reported a history of pregnancy termination. Women with a history of pregnancy termination were more often younger than 20 or older than 35 years, were more often nulliparous, of non-Dutch origin, of lower socioeconomic status and more often smoked (*Table 1*). The incidences of preterm delivery, cervical incompetence treated by cerclage, PIRP and PPH are shown in *Table 2*. Cervical incompetence treated by cerclage was more frequently present in the group with a history of pregnancy termination (0.2% versus 0.1%; $p < 0.001$). Preterm delivery, PIRP and PPH were also more common in the group with a history of pregnancy termination (respectively 4.9% versus 4.3%; $p < 0.001$; 3.6% versus 2.7%; $p < 0.001$; 5.0% versus 4.1%; $p < 0.001$). All associations remained statistically significant after adjustment for possible confounders. The strongest association was found between cervical incompetence treated by cerclage and pregnancy termination with an aOR of 4.6 (95% CI 2.9-7.2). The aORs for preterm delivery, PIRP and PPH were 1.11 (95% CI 1.02-1.20), 1.42 (95% CI 1.29-1.55) and 1.16 (95% CI 1.08-1.25), respectively. Any listed adverse outcome occurred in 10.9% of the 16,000 deliveries with a history of pregnancy termination versus 9.3% in the reference group, aOR 1.15 (95% CI 1.09-1.22). The absolute risk difference for any listed adverse outcome amounted 1.6% with a number needed to harm of 63 women.

A subgroup analysis in gestational age at delivery categories showed that previous termination of pregnancy had the strongest association with preterm delivery at early gestational ages (*Table 3*). The strongest association was found for delivery between 20⁺⁰ and 23⁺⁶ weeks, cOR 1.83 (95% CI 1.35-2.48) and aOR 1.61 (95% CI 1.13-2.30).

DISCUSSION

The most important finding of this study was that termination of pregnancy is associated with an increased risk for preterm delivery, cervical incompetence, placenta implantation/retention problems and postpartum hemorrhage in a subsequent singleton pregnancy.

In the study period, 90-95% of pregnancy terminations were performed surgically.¹³⁻¹⁴ We therefore assume that the observed increased risks are related to surgical abortion. Cervical dilatation for terminating pregnancy can damage the cervix and cause cervical incompetence, leading to preterm delivery.²³ This risk is, amongst others, dependent on gestational age at termination and extent of dilatation. Placental implantation and retention

problems are known to occur more often after uterine trauma such as previous caesarean delivery or uterine surgery.²⁶

A recent study in Scotland showed that surgical abortion was associated with a higher risk of preterm birth in a subsequent pregnancy than medicinal abortion.² The combined use of mifegyne and misoprostol is a safe medicinal alternative to surgical abortion but it is associated with a higher frequency of incomplete expulsion and longer post abortion bleeding.²⁷⁻²⁹ Therefore, after 8 weeks of pregnancy it is mainly performed in a clinical setting. Studies on patient preferences show a high acceptability for both procedures, although the acceptability of medicinal abortion declines with increasing gestational age.^{28,30}

Strengths and weaknesses of this study

The major strengths of this study are the size of the cohort, the uniform coverage of almost all deliveries nationwide, the standardized history taking in all obstetric practices and the accurate documentation of history and pregnancy complications.

A limitation of this study is that a history of pregnancy termination is probably selectively reported (i.e. underreported) by pregnant women. The relatively low prevalence of pregnancy termination in the history in our database compared to the Dutch abortion registry and another (urban, high-risk) cohort study further marks this.^{31,32} As a result, this will have weakened the observed associations found in our study, and may thus have led to an underestimation of the effects. In other words, the increased risk of complications in subsequent pregnancies after (surgical) abortion are probably even higher.

Another limitation is that curettage for spontaneous miscarriage is not registered in the PRN. This often does not require dilatation but the technique of uterine evacuation is the same. These women are now undetected in the reference group, leading to an underestimation of the effect of pregnancy termination on future reproduction. Furthermore, neither gestational age at the moment of pregnancy termination nor number of terminations nor the technique of termination were available in the registry. In the Netherlands 58% of pregnancy terminations are performed before 8 weeks.³¹

Comparison with other studies

Previous literature suggested a small but definitive risk for adverse outcome in pregnancies following surgical abortion. A recent systematic review of Lowit *et al* (3) reported an excess risk of preterm delivery of 5-12% (ORs 1.2-1.9) and an elevated risk of placenta praevia (ORs 1.3-1.7). More recently, a study of Bhattacharya *et al* (2) used similar methods and reported a higher risk of preterm birth and placental abruption in women with termination of pregnancy in their first pregnancy versus women who had a live birth in their first pregnancy (aOR 1.66 [95% CI 1.58-1.74] and 1.49 [95% CI 1.25-1.77] respectively). Another systematic

review and meta-analysis of Shah *et al* (6) described a further increased risk for preterm delivery in women after two or more terminations of pregnancy (one termination in history OR 1.36 [95% CI 1.24-1.50] and two or more terminations OR 1.93 [95% CI 1.28-2.71]. Haldre *et al* (8) studied the occurrence of placenta complications in deliveries following an abortion and found a higher risk of retained placenta (aOR 1.23 [95% CI 1.1-1.38]). The range in ORs could be related to gestational age at the moment of termination. Termination of pregnancy at a lower gestational age requires less cervical dilatation and therefore the risk of cervical damage may be lower.

Implications of the study

Women who have had a termination of pregnancy have an increased risk of preterm delivery, cervical incompetence treated by cerclage, placental problems and postpartum hemorrhage although absolute risks are low. Medicinal termination may be safer for future pregnancies than surgical termination. For future research we recommend to include the technique of pregnancy termination in perinatal registries, as well as gestational age at termination and number of terminations. The issue of possible harm to future reproduction is not routinely addressed when informing patients about various alternatives for terminating pregnancy. We recommend that this information should be included whenever there is a choice between both methods. The data generated in this study can be used for this purpose.

REFERENCES

1. Sedgh G, Singh S, Shah IH, Ahman E, Henshaw SK, Bankole A. Induced abortion: incidence and trends worldwide from 1995 to 2008. *Lancet* 2012;379:625-632.
2. Bhattacharya S, Lowit A, Bhattacharya S, Raja EA, Lee AJ, Mahmood T, et al. Reproductive outcomes following induced abortion: a national register-based cohort study in Scotland. *BMJ Open* 2012;2:e000911.doi:10.1136/bmjopen-2012-000911.
3. Lowit A, Bhattacharya S, Bhattacharya S. Obstetric performance following an induced abortion. *Best Pract Res Clin Obstet Gynaecol* 2010;24:667-682.
4. Freak-Poli R, Chan A, Tucker G, Street J. Previous abortion and risk of pre-term birth: a population study. *J Matern Fetal Neonatal Med* 2009;22(1):1-7.
5. Voigt M, Henrich W, Zygmunt M, Friese K, Straube S, Briese V. Is induced abortion a risk factor in subsequent pregnancy? *J Perinat. Med.* 2009;37:144-149.
6. Shah PS, Zao J. Induced termination of pregnancy and low birth weight and preterm birth: a systematic review and meta-analyses. *BJOG* 2009;116:1425-42.
7. Brown JS, Adera T, Masho SW. Previous abortion and the risk of low birth weight and preterm births. *J epidemiol Community Health* 2008;62:16-22.

8. Haldre K, Rahu K, Karro H, Rahu M. Previous history of surgically induced abortion and complications of the third stage of labour in subsequent normal vaginal deliveries. *J Matern Fetal Neonatal Med* 2008;21(12):884-888.

9. Reime B, Schücking BA, Wenzlaff P. Reproductive outcomes in adolescents who had a previous birth or an induced abortion compared to adolescents' first pregnancies. *BMC Pregnancy Childbirth* 2008; 8:4.

10. Chasen ST, Kalish RB, Gupta M, Kaufman J, Chervenak FA. Obstetric outcomes after surgical abortion at ≥ 20 weeks' gestation. *Am J Obstet Gynecol* 2005;193:1161-4.

11. Ancel PY, Lelong N, Papiernik E, Saurel-Cubizolles MJ, Kaminski M. History of induced abortion as a risk factor for preterm birth in European countries: results from the EUROPOP survey. *Hum Reprod* 2004;19:734-40.

12. Moreau C, Kaminski M, Ancel PY, Bouyer J, Escande B, Thiriez G. Previous induced abortions and the risk of very preterm delivery: results of the EPIPAGE study. *BJOG* 2005;112:430-7.

13. Lee L, Wijssen C. Annual report Abortion Registration 2006. Utrecht: Rutgers NissoGroep; 2007. Available from: http://www.rutgerswpf.nl/sites/default/files/rapport_LAR_2006.pdf

14. Lee L, Wijssen C. Annual report Abortion Registration 2007. Utrecht: Rutgers NissoGroep; 2008. (With a summary in English on page 7.) Available from: http://www.rutgerswpf.nl/sites/default/files/rapport_LAR_2007.pdf

15. Perinatreg.nl [internet]. Utrecht: The Netherlands Perinatal Registry. Available from: http://www.perinatreg.nl/home_english

16. Méray N, Reitsma JB, Ravelli AC, Bonsel GJ. Probabilistic record linkage is a valid and transparent tool to combine databases without a patient identification number. *J Clin Epidemiol.* 2007;60:883-91

17. Tromp M, Ravelli AC, Meray N, Reitsma JB, Bonsel GJ. An efficient validation method of probabilistic record linkage including readmissions and twins. *Methods Inf Med.* 2008;47:356-63

18. NVOG Richtlijn "Preventie recidief spontane vroeggeboorte" 2007. (Guideline Dutch Society of Obstetrics and Gynaecology: prevention relapse spontaneous preterm birth, March 2007). 2007. Utrecht. Available at: http://nvog-documenten.nl/index.php?pagina=/richtlijn/item/pagina.php&richtlijn_id=745. Accessed Jan 23, 2013.

19. Althuisius SM, Dekker GA, Geijn HP, Bekedam DJ, Hummel P. Cervical incompetence prevention randomized cerclage trial: study (CIPRACT). *Am J Obstet Gynecol* 2001;185:1107-1112.

20. Kwee A, Bots ML, Visser GHA, Bruinse HW. Emergency peripartum hysterectomy: A prospective study in the Netherlands. *Eur J Obstet Gynecol Reprod Biol* 2006;124:187-92.

21. Goldenberg R, Culhane JF, Lams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet* 2008; 371:75-84.
22. Raatikainen K, Heiskanen N, Heinonen S. Induced abortion: not an independent risk factor for pregnancy outcome, but a challenge for health counseling. *Ann Epidemiol* 2006;16:587-92.
23. Sheiner E, Sarid L, Levy A, Seidman DS, Hallak M. Obstetric risk factors and outcome of pregnancies complicated with early postpartum haemorrhage: a population-based study. *J Matern Fetal Neonatal Med* 2005; 18:149-154.
24. Iyasu S, Saftlas AK, Rowley DL, Koonin LM, Lawson HW, Atrash HK. The epidemiology of placenta previa in the United States, 1979 through 1987. *Am J Obstet Gynecol*. May 1993;68(5):1424-9.
25. Whitley KA, Trinchere K, Prutsman W, et al. Midtrimester dilation and evacuation versus prostaglandin induction: a comparison of composite outcomes. *Am J Obstet Gynecol* 2011;205:386.
26. Kwee A, Bots ML, Visser GHA, Bruinse HW. Obstetric management and outcome of pregnancy in women with a history of caesarean section in the Netherlands. *Eur J Obstet Gynecol Reprod Biol*. 2007;132:171-76.
27. Say L, Brahmi D, Kulier R, Campana A, Guimezoglu AM. Medical versus surgical methods for first trimester termination of pregnancy. *Cochrane Database of Systematic Reviews* 2002, Issue 4. Art. No.: CD003037. DOI: 10.1002/14651858.CD003037.pub2
28. Robson SC, Kelly T, Howel D, Deverill M, Hewison J, Lie MLS, Stamp E, Armstrong N, May CR. Randomised preference trial of medical versus surgical termination of pregnancy less than 14 weeks' gestation (TOPS). *Health Technol Assess* 2009;13(53).
29. Graziosi GCM, Mol BWJ, Reuwer PJH, Drogtop A, Bruinse HW. Misoprostol versus curettage in women with early pregnancy failure after initial expectant management: a randomized trial. *Hum Reprod* 2004;19(8):1894-9.
30. Rørbye C, Nørgaard M, Nilas L. Medical versus surgical abortion: comparing satisfaction and potential confounders in a partly randomized study. *Hum. Reprod*. 2005;20:834-838.
31. The Health Care Inspectorate. Annual report 2009 Termination of Pregnancy Act. The Hague; 2010 (with a summary in English on page 29).
32. Vrijkotte T.G.M. (2012). Amsterdam Born Children and their Development (ABCD Study). Unpublished raw data.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Figure 1. Patient selection

Preterm delivery: gestation age from 20 to 37 weeks. CI treated by cerclage: cervical incompetence treated by cerclage. PIRP (placenta implantation and retention problems): placenta praevia, placental abruption or retained placenta.

For peer review only

Table 1. Patient characteristics

Characteristics	Termination of pregnancy in history (%)	Reference group (%)
Study population	16.000	1.341.894
Maternal age^a		
Mean (SD)	30,41 (5,762)	30,40 (4,839)
<20	525 (3,3)	22.786 (1,7)
20 – 25	2.983 (18,6)	187.355 (14)
26 – 30	4.085 (25,5)	447.307 (33,3)
31 – 35	5.186 (32,4)	495.546 (36,9)
> 35	3.219 (20,1)	188.591 (14,1)
Parity^a		
0	9.265 (57,9)	613.755 (45,7)
1	4.692 (29,3)	485.287 (36,2)
2	1.453 (9,1)	169.802 (12,7)
3	417 (2,6)	46.910 (3,5)
≥ 4	172 (1,1)	25.822 (1,9)
SES^{a,b}		
High	3.469 (21,7)	314.667 (23,4)
Normal	5.488 (34,3)	608.113 (45,3)
Low	6.861 (43,0)	402.254 (30,0)
Ethnicity^a		
Dutch	10.304 (64,4)	1.093.438 (81,5)
Mediterranean	1.184 (7,4)	105.368 (7,9)
Other European	1.012 (6,3)	33.728 (2,5)
Creole	1.441 (9,0)	30.226 (2,3)
Hindu	341 (2,1)	14.523 (1,1)
Asian	605 (3,8)	24.408 (1,8)
Other	1.086 (6,8)	31.519 (2,3)
Smoking ^a	180 (1,1)	5.712 (0,4)
Drug dependence ^a	91 (0,6)	1.232 (0,09)
Reproductive history		
Preterm delivery ^a	165 (1,0)	16.122 (1,2)
Cervical incompetence/ Shirodkarprocedure	3 (0,02)	381 (0,03)
Placenta praevia ^a	8 (0,05)	183 (0,01)
Placental abruption	17 (0,1)	2023 (0,2)
Manual removal of the placenta	75 (0,5)	7.353 (0,5)
Postpartum Haemorrhage ^a	156 (1,0)	19.062 (1,4)
Cesarean section ^a	839 (5,2)	101.884 (7,6)
Cervical surgery ^a	28 (0,2)	1.424 (0,1)
Uterine myoma ^a	79 (0,5)	4.732 (0,4)
Myomectomy subserous	5 (0,03)	257 (0,02)
Myomectomy submucous/intramural	4 (0,03)	409 (0,03)
Index gravidity		
Pyelitis ^a	20 (0,1)	736 (0,05)
Polyhydramnios	5 (0,03)	234 (0,02)
Mode of delivery^a		
Spontaneous vaginal delivery	12.048 (75,4)	1.024.044 (76,4)
Instrumental vaginal delivery	1.682 (10,5)	143.654 (10,7)
Elective caesarean delivery	738 (4,6)	70.345 (5,2)
Emergency caesarean delivery	1.520 (9,5)	102.090 (7,6)
Perinatal mortality ^a	109 (0,7)	7602 (0,6)

^a P value < 0.05, ^b socioeconomic status (SES)

Table 2. Pregnancy outcomes in patients with and without a history of pregnancy termination.

Outcome	Termination of pregnancy in history (%)	Reference group (%)	Risk difference	NNH	cOR (95% CI)	aOR (95% CI)
Cervical incompetence treated by cerclage	39 (0,2)	712 (0,1)	0,1	1000	4.60 (3.33-6.36)	4.58 (2.93-7.15)
Preterm birth	781 (4,9)	57.019 (4,3)	0,6	167	1.15 (1.07-1.23)	1.11 (1.02-1.20)
PIRP	571 (3,6)	35.822 (2,7)	0,9	111	1.35 (1.25-1.47)	1.32 (1.21-1.43)
Placenta praevia	41 (0,3)	1.315 (0,1)	0,2	500	2.62 (1.92-3.58)	2.48 (1.80-3.42)
Placental abruption	22 (0,1)	1.074 (0,1)	0	-	1.72 (1.13-2.62)	1.56 (1.02-2.39)
Retained placenta	512 (3,2)	33.521 (2,5)	0,7	142	1.30 (1.19-1.42)	1.26 (1.15-1.38)
Postpartum Haemorrhage	760 (5,0)	53.571 (4,1)	0,9	111	1.22 (1.14-1.32)	1.16 (1.08-1.25)
Any listed adverse outcome	1.750 (10,9)	124.586 (9,3)	1,6	63	1.20 (1.14-1.26)	1.15 (1.09-1.22)
Any listed adverse outcome other than cervical incompetence treated by cerclage	1.726 (10,8)	124.119 (9,2)	1,6	63	1.19 (1.13-1.25)	1.14 (1.08-1.21)

P-value for all outcomes < 0.001
Preterm birth (PB)= gestation age from 20 to 37 weeks, PIRP= placenta implantation or retention problems, NNH = number needed to harm, crude odds ratio (cOR) and adjusted odds ratio (aOR). aOR: OR are adjusted for known confounders for the given outcome. PB and cervical incompetence treated by cerclage are adjusted for maternal age, ethnicity, socioeconomic status (SES), parity, smoking, drug dependence, pyelitis, polyhydramnios and in history: PB, cervix incompetence and/or Shirodkarprocedure, uterine myoma and cervical surgery. aOR PIRP, placenta praevia, placental abruption and retained placenta are adjusted for maternal age, ethnicity, SES, parity, smoking, drug dependence and in history: cesarean section and PIRP. aOR PPH is adjusted for maternal age, ethnicity, SES, parity, polyhydramnios and in history: PPH and uterine myoma. aOR Composite outcome is adjusted for all the above mentioned.

Table 3. Gestational age at delivery in women with and without a history of pregnancy termination.

Gestational age (weeks)	Termination of pregnancy in history (%)	Reference group (%)	cOR (95%CI)	aOR (95%CI)
20 ⁺⁰ - 23 ⁺⁶	43 (0,3)	1966 (0,1)	1.83 (1.35-2.48)	1.61 (1.13-2.30)
24 ⁺⁰ - 28 ⁺⁶	56 (0,4)	2658 (0,2)	1.76 (1.35-2.30)	1.67 (1.22-2.28)
29 ⁺⁰ - 32 ⁺⁶	80 (0,5)	5393 (0,4)	1.24 (0.99-1.55)	1.36 (1.07-1.74)
33 ⁺⁰ - 36 ⁺⁶	602 (3,8)	47.002 (3,5)	1.07 (0.99-1.16)	1.04 (0.95-1.14)
≥ 37	15.152 (95,1)	1.268.013 (95,7)	Reference group	Reference group

aOR are adjusted for maternal age, ethnicity, SES, parity, smoking, drug dependence, pyelitis, polyhydramnios, uterine myoma, cervical surgery and in history: preterm birth, cervix incompetence and/or Shirodkarprocedure.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Other Information

Funding:

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

No conflict of interest declaration:

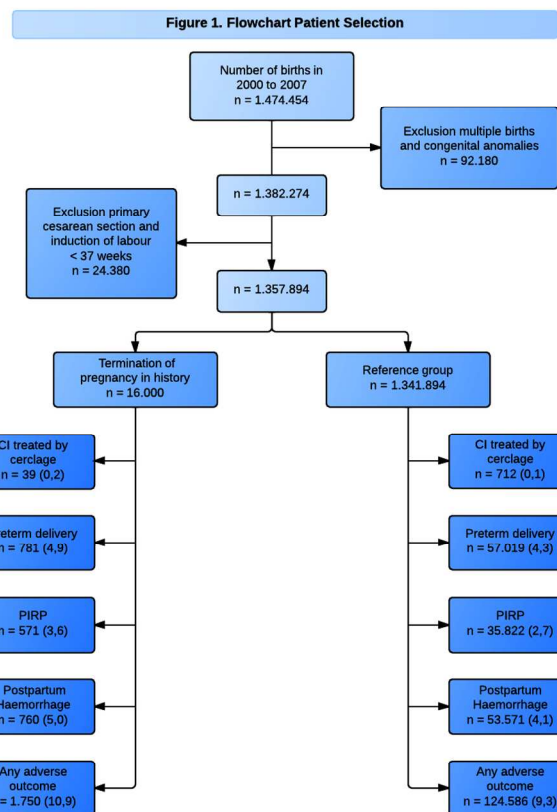
"All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work."

Details of Contributors:

GCMLPC and AF initiated the study. BLS, GCMLPC, MPHK were involved in designing the study. BLS collected the data. BLS, MPHK, CWPMH analysed the data. All authors actively participated in interpreting the results and revising the paper, which was written by BLS, GCMLP, MPHK, AF and CWPMH.

Ethical approval: The board and privacy commission of the Netherlands Perinatal Registry approved this study.

Data sharing: Dataset is available on the Netherlands Perinatal Registry. Consent was not obtained, but presented data are anonymised.



Preterm delivery: gestation age from 20 to 37 weeks. CI treated by cerclage: cervical incompetence treated by cerclage. PIRP (placenta implantation and retention problems): placenta praevia, placental abruption or retained placenta.

479x620mm (72 x 72 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4,5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4,5
		(b) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4,5
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5
		(b) Describe any methods used to examine subgroups and interactions	5
		(c) Explain how missing data were addressed	N/A
		(d) If applicable, explain how loss to follow-up was addressed	N/A
		(e) Describe any sensitivity analyses	5
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) Summarise follow-up time (eg, average and total amount)	4,5
Outcome data	15*	Report numbers of outcome events or summary measures over time	6
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 2
		(b) Report category boundaries when continuous variables were categorized	6
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	6
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6, table 3
Discussion			
Key results	18	Summarise key results with reference to study objectives	6
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8
Generalisability	21	Discuss the generalisability (external validity) of the study results	7,8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	N/A

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.



The influence of pregnancy termination on the outcome of subsequent pregnancies: retrospective cohort study

Journal:	<i>BMJ Open</i>
Manuscript ID:	bmjopen-2013-002803.R1
Article Type:	Research
Date Submitted by the Author:	23-Apr-2013
Complete List of Authors:	Scholten, Brenda; University Medical Center Utrecht, Obstetrics Page-Christiaens, Godelieve; University Medical Center Utrecht, Obstetrics Franx, Arie; University Medical Center Utrecht, Obstetrics Hukkelhoven, Chantal; Netherlands Perinatal Registry, Koster, Maria; University Medical Center Utrecht, Obstetrics
Primary Subject Heading:	Obstetrics and gynaecology
Secondary Subject Heading:	Obstetrics and gynaecology
Keywords:	termination of pregnancy, preterm delivery, cervical incompetence, placenta praevia, placental abruption, retained placenta

SCHOLARONE™
Manuscripts

Title page

The influence of pregnancy termination on the outcome of subsequent pregnancies: retrospective cohort study	Title
Brenda L Scholten, Godelieve C M L Page-Christiaens, Arie Franx, Chantal W P M Hukkelhoven, Maria P H Koster	Author's name
University Medical Center Utrecht, Lundlaan 6, 3584 EA, Utrecht, PO box 85090, 3508 AB, Utrecht, The Netherlands Brenda Scholten, MSc Department of Obstetrics, University Medical Center Utrecht, Godelieve Page-Christiaens, gynaecologist Department of Obstetrics, University Medical Center Utrecht, Arie Franx, professor of Obstetrics Netherlands Perinatal Registry, Mercatorlaan 1200, Room 46 PO box8588, 3503 RN, Utrecht, The Netherlands, Chantal Hukkelhoven, epidemiologist Department of Obstetrics, University Medical Center Utrecht, Maria Koster, epidemiologist	Address for each author
Godelieve Page-Christiaens, University Medical Center Utrecht, Lundlaan 6, Room KE 04.123.1, PO box 85090, 3508 AB Utrecht, The Netherlands, L.Christiaens@umcutrecht.nl Tel +31 88 755 6426, Fax +31 88 755 5320	Corresponding author
Termination of pregnancy, cervical incompetence, preterm delivery, placenta implantation and retention problems	Keywords
2.053	Word count

Abstract

Objective: To compare the incidences of preterm delivery, cervical incompetence treated by cerclage, placenta implantation or retention problems (i.e. placenta praevia, placental abruption and retained placenta) and postpartum haemorrhage between women with and without a history of pregnancy termination.

Design: Retrospective cohort study using aggregated data from a national perinatal registry.

Setting: All midwifery practices and hospitals in the Netherlands.

Participants: All pregnant women with a singleton pregnancy without congenital malformations and a gestational age of ≥ 20 weeks who delivered between January 2000 and December 2007.

Main outcome measures: Preterm delivery, cervical incompetence treated by cerclage, placenta praevia, placental abruption, retained placenta and postpartum haemorrhage

Results: A previous pregnancy termination was reported in 16.000 (1.2%) deliveries. The vast majority of these (90-95%) were done by surgical methods. The incidence of all outcome measures was significantly higher in women with a history of pregnancy termination. Adjusted odds ratios (95% confidence interval) for cervical incompetence treated by cerclage, preterm delivery, placenta implantation or retention problems and postpartum haemorrhage were 4.6 (2.9-7.2), 1.11 (1.02-1.20), 1.42 (1.29-1.55) and 1.16 (1.08-1.25), respectively. Associated numbers needed to harm were 1000, 167, 111 and 111, respectively. For any listed adverse outcome the number needed to harm was 63.

Conclusions: In this large nationwide cohort study we found a positive association between surgical termination of pregnancy and subsequent preterm delivery, cervical incompetence treated by cerclage, placenta implantation or retention problems and postpartum haemorrhage in a subsequent pregnancy. Absolute risks for these outcomes however remain small. Medicinal termination might be considered first whenever there is a choice between both methods.

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Article Summary

Article focus

- To estimate the influence of pregnancy termination on the outcome of subsequent pregnancies.
- Does termination of pregnancy lead to cervical incompetence and/or preterm delivery in subsequent pregnancies?
- Is termination of pregnancy associated with a higher risk of placenta implantation or retention problems (i.e. placenta praevia, placental abruption and retained placenta) in a subsequent pregnancy?

Key Messages

- Surgical termination of pregnancy is positively associated with subsequent spontaneous preterm delivery, cervical incompetence treated by cerclage, placenta implantation/retention problems and postpartum hemorrhage in a subsequent singleton pregnancy.

Strengths and limitations of this study

- One of the largest cohort studies on reproductive outcomes of women with and without a history of pregnancy termination.
- Registration of and adjustment for many potential confounders.
- The perinatal registry contains no information on the technique of pregnancy termination.
- The number of and gestational age at pregnancy terminations in a given woman was not registered
- Underreporting of pregnancy termination leads to an underestimation of its effect on future reproduction.

INTRODUCTION

Worldwide each year at least 43 million pregnancies are terminated, often in young nulliparous women.¹ Data on the effect on future pregnancies suggest an increase in risk for complications in subsequent pregnancies after pregnancy termination.²⁻¹³

In the Netherlands, approximately 32.000 pregnancies are terminated each year.¹⁴ The abortion rate has been unchanged since 2001 with 8.8 per thousand women of childbearing age (15 to 44 years) resident in the Netherlands having a pregnancy terminated each year.¹⁴ The vast majority (90-95%) of these abortions are performed in specialized clinics by surgical methods namely vacuum aspiration and curettage.¹⁴⁻¹⁵ In 1999, medicinal abortion with a combination of antiprogestagens and prostaglandins has been introduced in clinical practice. However, in the Netherlands this method is mainly used for termination of pregnancy for medical or genetic reasons and usually not offered as an alternative to women requesting abortion for nonmedical reasons.

The question arises how women should be counseled as to the effect of surgical abortion on future reproductive performance. We therefore set out to compare the incidences of 1) preterm delivery, 2) cervical incompetence treated by cerclage, 3) placenta implantation or retention problems (PIRP) which include placenta praevia, placental abruption and retained placenta and 4) postpartum hemorrhage (PPH) in pregnancies of women with and without a history of pregnancy termination.

METHODS

Study population

Prospectively collected data were derived from the Netherlands Perinatal Registry (PRN).¹⁶ The PRN is a Dutch nationwide database that contains demographics and information about mother and newborn, course and outcome of pregnancy, and content and organization of care, all entered by health care providers. Around 96% of all deliveries from 20 weeks of gestation onwards are registered in the PRN. The database consists of three linked and validated registries: the national obstetric database for midwives (LVR-1), the national obstetric database for gynecologists (LVR-2) and the national neonatal/pediatric database (LNR).¹⁷⁻¹⁸ The study period was from January 2000 till and including December 2007. We chose this period to avoid byass, because medicinal termination of pregnancy was not commonly used at that time, the majority of pregnancy terminations being done surgically. All multiple births and births of a child with a congenital anomaly in index pregnancies were excluded. Also all women where labor was induced or a planned caesarean section was performed before 37 weeks gestation, i.e. iatrogenic preterm deliveries, were excluded (*Figure 1*). Whether there had been a previous termination of pregnancy or not was registered based on responses given by the pregnant woman in a predefined pregnancy

intake questionnaire, amongst others on reproductive history. In Dutch different terminology is used for pregnancy termination as opposed to miscarriage. This questionnaire is being filled out at the first prenatal visit, usually around 12 weeks of pregnancy. The number of pregnancy terminations in an individual woman is not registered in the PRN. The primary study outcomes were preterm delivery, cervical incompetence with placement of a cerclage, PIRP and PPH.

Definitions

Preterm delivery was registered from 20 weeks on and we therefore for this study defined preterm delivery as delivery between 20 and 37 weeks of gestation. The aim of the study was to document any registered possible adverse effects. For a subgroup analysis of gestational age at delivery we divided gestational age into 5 groups: 20⁺⁰ to 23⁺⁶ weeks, 24⁺⁰ to 28⁺⁶ weeks, 29⁺⁰ to 32⁺⁶ weeks, 33⁺⁰ to 36⁺⁶ weeks and 37 weeks and later. In the Netherlands a cervical cerclage is considered to be indicated when there is shortening or dilatation of the cervix without contractions during the second trimester of pregnancy.^{19,20} A history of pregnancy termination is not a reason for cerclage.

Placenta praevia, placental abruption and retained placenta have been merged into the composite measure PIRP because of the low incidence of these outcomes. Retained placenta also includes postpartum curettage for incomplete placenta. PPH was defined as more than 1000 milliliters estimated blood loss postpartum.

Prior cervical surgery includes conization or amputation of the cervix. Polyhydramnios was defined as an estimated amount of amniotic fluid of more than two liters, diagnosed by ultrasound during pregnancy.²¹ Perinatal mortality was defined as stillbirth or death up to 7 days after birth, after a gestation period of at least 22 weeks (WHO definition).

Socioeconomic status (SES) was based on the average income level of the neighborhood, which was determined by the first four digits of the woman's postal code, a common method for establishing SES in the Netherlands.

Statistical analysis

We used t-tests and chi-square tests to compare baseline characteristics and the difference in incidence of outcome measures between both groups. Logistic regression analysis was performed to calculate crude odds ratios (cOR) and adjusted odds ratios (aOR) and their 95% confidence intervals (95% CI). Odds ratios were adjusted for variables that are considered as possible confounders in the literature: maternal age, gravidity, parity, SES, ethnicity, smoking, drug dependence, pyelitis, polyhydramnios, current uterus myomatosis, history of preterm delivery, history of cervical incompetence, history of placenta praevia,

history of placental abruption, history of manual removal of the placenta, history of PPH (not due perineal trauma) and history of cervical surgery.²²⁻²⁷

A subgroup analysis of various categories of gestational age was performed for the outcome preterm delivery because a deleterious effect of cervical dilatation at time of delivery could be larger at early gestational ages.

We computed a number needed to harm (1/risk difference) in which the risk difference equaled the estimated incidence in women with a history of pregnancy termination minus the incidence among women without a history of pregnancy termination. All analyses were done using SPSS version 19. Ethical approval was obtained from the board and privacy commission of the Netherlands Perinatal Registry.

RESULTS

During the study period 1,357,894 singletons were born who fulfilled the selection criteria (*Figure 1*). In 16,000 deliveries (1.2%) the mother reported a history of pregnancy termination. Women with a history of pregnancy termination were more often younger than 20 or older than 35 years, were more often nulliparous, of non-Dutch origin, of lower socioeconomic status and more often smoked (*Table 1*). The incidences of preterm delivery, cervical incompetence treated by cerclage, PIRP and PPH are shown in *Table 2*. Cervical incompetence treated by cerclage was more frequently present in the group with a history of pregnancy termination (0.2% versus 0.1%; $p < 0.001$). Preterm delivery, PIRP and PPH were also more common in the group with a history of pregnancy termination. All associations remained statistically significant after adjustment for possible confounders. The strongest association was found between cervical incompetence treated by cerclage and pregnancy termination with an aOR of 4.6 (95% CI 2.9-7.2). The aORs for preterm delivery, PIRP and PPH are shown in *Table 2*. Any listed adverse outcome occurred in 10.9% of the 16,000 deliveries with a history of pregnancy termination versus 9.3% in the reference group, aOR 1.15 (95% CI 1.09-1.22). The absolute risk difference for any listed adverse outcome amounted 1.6% with a number needed to harm of 63 women.

A subgroup analysis in gestational age at delivery categories showed that previous termination of pregnancy had the strongest association with preterm delivery at early gestational ages (*Table 3*). The strongest association was found for delivery between 20⁺⁰ and 23⁺⁶ weeks, cOR 1.83 (95% CI 1.35-2.48) and aOR 1.61 (95% CI 1.13-2.30).

DISCUSSION

The most important finding of this study was that termination of pregnancy is associated with an increased risk for preterm delivery, cervical incompetence, placenta implantation/retention problems and postpartum hemorrhage in a subsequent singleton pregnancy.

In the study period, 90-95% of pregnancy terminations were performed surgically.¹⁴⁻¹⁵ We therefore assume that the observed increased risks are related to surgical abortion. Cervical dilatation for terminating pregnancy can damage the cervix and cause cervical incompetence, leading to preterm delivery.²⁸ This risk is, amongst others, dependent on gestational age at termination and extent of dilatation. Placental implantation and retention problems are known to occur more often after uterine trauma such as previous caesarean delivery or uterine surgery.²⁹

A recent study in Scotland showed that surgical abortion was associated with a higher risk of preterm birth in a subsequent pregnancy than medicinal abortion.² The combined use of mifegyne and misoprostol is a safe medicinal alternative to surgical abortion but it is associated with a higher frequency of incomplete expulsion and longer post abortion bleeding.³⁰⁻³² Therefore, after 8 weeks of pregnancy it is mainly performed in a clinical setting. Studies on patient preferences show a high acceptability for both procedures, although the acceptability of medicinal abortion declines with increasing gestational age.^{31,33}

Strengths and weaknesses of this study

The major strengths of this study are the size of the cohort, the uniform coverage of almost all deliveries nationwide, the standardized history taking in all obstetric practices and the accurate documentation of history and pregnancy complications.

A limitation of this study is that a history of pregnancy termination is probably selectively reported (i.e. underreported) by pregnant women. The relatively low prevalence of pregnancy termination in the history in our database compared to the Dutch abortion registry and another (urban, high-risk) cohort study further marks this.^{34,35} Presuming that women who did not report to have had a history of termination had the same risk of adverse outcome as those who did report this, underreporting has most likely weakened the associations in our study..

Secondly, some women have delivered more than once during the study period, and the sequence of various pregnancy outcomes is not known. Women may therefore have multiple records in the registry. These records cannot be linked to one another in the PRN data yet and therefore no adjustment could be made.

Another limitation is that curettage for spontaneous miscarriage is not registered in the PRN. This often does not require dilatation but the technique of uterine evacuation is the same. These women are now undetected in the reference group, leading to an underestimation of the effect of intrauterine manipulation on future reproduction. Furthermore, neither

gestational age at the moment of pregnancy termination nor number of terminations nor the technique of termination were available in the registry. In the Netherlands 58% of pregnancy terminations are performed before 8 weeks. In two thirds of the women registered in the (legally required) abortion registry it was the first termination, one quarter had had one previous termination and the remaining group had had 2 or more previous terminations.³⁴

Comparison with other studies

Previous literature suggested a small but definitive risk for adverse outcome in pregnancies following surgical abortion. The large study of Bhattacharya *et al* (2) used similar methods as we did and reported a higher risk of preterm birth and placental abruption in women with termination of pregnancy in their first pregnancy (n=67,745) versus women who had a live birth in their first pregnancy (n=357,080) (aOR 1.66 [95% CI 1.58-1.74] and 1.49 [95% CI 1.25-1.77] respectively). More recently Klemitt *et al* (3) studied over 300.000 first time mothers from a 12 year period in the Medical Birth Register and linked their data to a 25 year period in the Finnish Abortion Registry. They found an association between preterm birth and previous abortion, with worse outcomes after multiple abortions. The abortion rate in Finland is similar to the one in the Netherlands.³⁴ A recent systematic review of Lowit *et al* (4) reported an excess risk of preterm delivery of 5-12% (ORs 1.2-1.9) and an elevated risk of placenta praevia (ORs 1.3-1.7). Another systematic review and meta-analysis of Shah *et al* (6) described a further increased risk for preterm delivery in women after two or more terminations of pregnancy (one termination in history OR 1.36 [95% CI 1.24-1.50] and two or more terminations OR 1.93 [95% CI 1.28-2.71]. Haldre *et al* (8) studied the occurrence of placenta complications in deliveries following an abortion and found a higher risk of retained placenta (aOR 1.23 [95% CI 1.1-1.38]). The range in ORs could be related to gestational age at the moment of termination. Termination of pregnancy at a lower gestational age requires less cervical dilatation and therefore the risk of cervical damage may be lower.

Implications of the study

Women who have had a termination of pregnancy have an increased risk of preterm delivery, cervical incompetence treated by cerclage, placental problems and postpartum hemorrhage although absolute risks are low. Medicinal termination may be safer for future pregnancies than surgical termination. For future research we recommend to include the technique of pregnancy termination in perinatal registries, as well as gestational age at termination and number of terminations. The issue of possible harm to future reproduction is not routinely addressed when informing patients about various alternatives for terminating pregnancy. We recommend that this information should be included whenever there is a choice between both methods. The data generated in this study can be used for this purpose.

REFERENCES

1. Sedgh G, Singh S, Shah IH, et al. Induced abortion: incidence and trends worldwide from 1995 to 2008. *Lancet* 2012;379:625-632.

2. Bhattacharya S, Lowit A, Bhattacharya S, et al. Reproductive outcomes following induced abortion: a national register-based cohort study in Scotland. *BMJ Open* 2012;2:e000911.doi:10.1136/bmjopen-2012-000911.

3. Klemetti K, Gissler M, Niinimäki M, et al. Birth outcomes after induced abortion: a nationwide register-based study of births in Finland. *Hum Reprod* 2012; 27(11): 3315-20.

4. Lowit A, Bhattacharya S, Bhattacharya S. Obstetric performance following an induced abortion. *Best Pract Res Clin Obstet Gynaecol* 2010;24:667-682.

5. Freak-Poli R, Chan A, Tucker G, et al. Previous abortion and risk of pre-term birth: a population study. *J Matern Fetal Neonatal Med* 2009;22(1):1-7.

6. Voigt M, Henrich W, Zygmunt M, et al. Is induced abortion a risk factor in subsequent pregnancy? *J Perinat. Med.* 2009;37:144-149.

7. Shah PS, Zao J. Induced termination of pregnancy and low birth weight and preterm birth: a systematic review and meta-analyses. *BJOG* 2009;116:1425-42.

8. Brown JS, Adera T, Masho SW. Previous abortion and the risk of low birth weight and preterm births. *J epidemiol Community Health* 2008;62:16-22.

9. Haldre K, Rahu K, Karro H, et al. Previous history of surgically induced abortion and complications of the third stage of labour in subsequent normal vaginal deliveries. *J Matern Fetal Neonatal Med* 2008;21(12):884-888.

10. Reime B, Schücking BA, Wenzlaff P. Reproductive outcomes in adolescents who had a previous birth or an induced abortion compared to adolescents' first pregnancies. *BMC Pregnancy Childbirth* 2008; 8:4.

11. Chasen ST, Kalish RB, Gupta M, et al. Obstetric outcomes after surgical abortion at ≥ 20 weeks' gestation. *Am J Obstet Gynecol* 2005;193:1161-4.

12. Ancel PY, Lelong N, Papiernik E, et al. History of induced abortion as a risk factor for preterm birth in European countries: results from the EUROPOP survey. *Hum Reprod* 2004;19:734-40.

13. Moreau C, Kaminski M, Ancel PY, et al. Previous induced abortions and the risk of very preterm delivery: results of the EPIPAGE study. *BJOG* 2005;112:430-7.

14. Lee L, Wijzen C. Annual report Abortion Registration 2006. Utrecht: Rutgers NissoGroep; 2007. Available from: http://www.rutgerswpf.nl/sites/default/files/rapport_LAR_2006.pdf

15. Lee L, Wijzen C. Annual report Abortion Registration 2007. Utrecht: Rutgers NissoGroep; 2008. (With a summary in English on page 7.) Available from: http://www.rutgerswpf.nl/sites/default/files/rapport_LAR_2007.pdf

16. Perinatreg.nl [internet]. Utrecht: The Netherlands Perinatal Registry. Available from: http://www.perinatreg.nl/home_english
17. Méray N, Reitsma JB, Ravelli AC, et al. Probabilistic record linkage is a valid and transparent tool to combine databases without a patient identification number. *J Clin Epidemiol*. 2007;60:883-91
18. Tromp M, Ravelli AC, Meray N, et al. An efficient validation method of probabilistic record linkage including readmissions and twins. *Methods Inf Med*. 2008;47:356-63
19. NVOG Richtlijn "Preventie recidief spontane vroeggeboorte" 2007. (Guideline Dutch Society of Obstetrics and Gynaecology: prevention relapse spontaneous preterm birth, March 2007). 2007. Utrecht. Available at: http://nvog-documenten.nl/index.php?pagina=/richtlijn/item/pagina.php&richtlijn_id=745. Accessed Jan 23, 2013.
20. Althuisius SM, Dekker GA, Geijn HP, et al. Cervical incompetence prevention randomized cerclage trial: study (CIPRACT). *Am J Obstet Gynecol* 2001;185:1107-1112.
21. Croom CS, Baniyas BB, Ramos-Santos E, et al. Do semiquantitative amniotic fluid indexes reflect actual volume? *Am J Obstet Gynecol*. 1992 Oct;167(4 Pt 1):995-9
22. Kwee A, Bots ML, Visser GHA, et al. Emergency peripartum hysterectomy: A prospective study in the Netherlands. *Eur J Obstet Gynecol Reprod Biol* 2006;124:187-92.
23. Goldenberg R, Culhane JF, Lams JD, et al. Epidemiology and causes of preterm birth. *Lancet* 2008; 371:75-84.
24. Raatikainen K, Heiskanen N, Heinonen S. Induced abortion: not an independent risk factor for pregnancy outcome, but a challenge for health counseling. *Ann Epidemiol* 2006;16:587-92.
25. Sheiner E, Sarid L, Levy A, et al. Obstetric risk factors and outcome of pregnancies complicated with early postpartum haemorrhage: a population-based study. *J Matern Fetal Neonatal Med* 2005; 18:149-154.
26. Iyasu S, Saftlas AK, Rowley DL, et al. The epidemiology of placenta previa in the United States, 1979 through 1987. *Am J Obstet Gynecol*. May 1993;68(5):1424-9.
27. Schaaf JM, Ravelli CJ, Mol BWJ, et al. Development of a prognostic model for predicting spontaneous singleton preterm birth. *Eur J Obstet Gynecol Reprod Biol* 2012; 164:150-155.
28. Whitley KA, Trinchere K, Prutsman W, et al. Midtrimester dilation and evacuation versus prostaglandin induction: a comparison of composite outcomes. *Am J Obstet Gynecol* 2011;205:386.
29. Kwee A, Bots ML, Visser GHA, et al. Obstetric management and outcome of pregnancy in women with a history of caesarean section in the Netherlands. *Eur J Obstet Gynecol Reprod Biol*. 2007;132:171-76.

30. Say L, Brahmi D, Kulier R, et al. Medical versus surgical methods for first trimester termination of pregnancy. Cochrane Database of Systematic Reviews 2002, Issue 4. Art. No.: CD003037. DOI: 10.1002/14651858.CD003037.pub2

31. Robson SC, Kelly T, Howel D, et al. Randomised preference trial of medical versus surgical termination of pregnancy less than 14 weeks' gestation (TOPS). Health Technol Assess 2009;13(53).

32. Graziosi GCM, Mol BWJ, Reuwer PJH, et al. Misoprostol versus curettage in women with early pregnancy failure after initial expectant management: a randomized trial. Hum Reprod 2004;19(8):1894-9.

33. Rørbye C, Nørgaard M, Nilas L. Medical versus surgical abortion: comparing satisfaction and potential confounders in a partly randomized study. Hum. Reprod. 2005;20:834–838.

34. The Health Care Inspectorate. Annual report 2009 Termination of Pregnancy Act. The Hague; 2010 (with a summary in English on page 29).

35. Vrijkotte T.G.M. (2012). Amsterdam Born Children and their Development (ABCD Study). Unpublished raw data.

Figure 1. Patient selection

Preterm delivery: delivery at a gestational age between 20 and 37 weeks. CI treated by cerclage: cervical incompetence treated by cerclage. PIRP (placenta implantation and retention problems): placenta praevia, placental abruption or retained placenta.

Table 1. Patient characteristics

Characteristics	Termination of pregnancy in history (%)	Reference group (%)
Study population	16.000	1.341.894
Maternal age^a		
Mean (SD)	30,41 (5,8)	30,40 (4,8)
<20	525 (3,3)	22.786 (1,7)
20 – 25	2.983 (18,6)	187.355 (14)
26 – 30	4.085 (25,5)	447.307 (33,3)
31 – 35	5.186 (32,4)	495.546 (36,9)
> 35	3.219 (20,1)	188.591 (14,1)
Parity^a		
0	9.265 (57,9)	613.755 (45,7)
1	4.692 (29,3)	485.287 (36,2)
2	1.453 (9,1)	169.802 (12,7)

3	417 (2,6)	46.910 (3,5)
≥ 4	172 (1,1)	25.822 (1,9)
SES^{a,b}		
High	3.469 (21,7)	314.667 (23,4)
Normal	5.488 (34,3)	608.113 (45,3)
Low	6.861 (43,0)	402.254 (30,0)
Ethnicity^a		
Dutch	10.304 (64,4)	1.093.438 (81,5)
Mediterranean	1.184 (7,4)	105.368 (7,9)
Other European	1.012 (6,3)	33.728 (2,5)
Creole	1.441 (9,0)	30.226 (2,3)
Hindu	341 (2,1)	14.523 (1,1)
Asian	605 (3,8)	24.408 (1,8)
Other	1.086 (6,8)	31.519 (2,3)
Smoking ^a	180 (1,1)	5.712 (0,4)
Drug dependence ^a	91 (0,6)	1.232 (0,09)
Reproductive history		
Preterm delivery ^a	165 (1,0)	16.122 (1,2)
Cervical incompetence/ Shirodkarprocedure	3 (0,02)	381 (0,03)
Placenta praevia ^a	8 (0,05)	183 (0,01)
Placental abruption	17 (0,1)	2023 (0,2)
Manual removal of the placenta	75 (0,5)	7.353 (0,5)
Postpartum Haemorrhage ^a	156 (1,0)	19.062 (1,4)
Cesarean section ^a	839 (5,2)	101.884 (7,6)
Cervical surgery ^a	28 (0,2)	1.424 (0,1)
Uterine myoma ^a	79 (0,5)	4.732 (0,4)
Myomectomy subserous	5 (0,03)	257 (0,02)
Myomectomy submucous/intramural	4 (0,03)	409 (0,03)
Index gravidity		
Pyelitis ^a	20 (0,1)	736 (0,05)
Polyhydramnios	5 (0,03)	234 (0,02)
Mode of delivery^a		
Spontaneous vaginal delivery	12.048 (75,4)	1.024.044 (76,4)
Instrumental vaginal delivery	1.682 (10,5)	143.654 (10,7)
Elective caesarean delivery	738 (4,6)	70.345 (5,2)
Emergency caesarean delivery	1.520 (9,5)	102.090 (7,6)
Perinatal mortality ^a	109 (0,7)	7602 (0,6)
^a P value < 0.05, ^b socioeconomic status (SES)		

Table 2. Pregnancy outcomes in patients with and without a history of pregnancy termination.

Outcome	Termination of pregnancy in history (%)	Reference group (%)	Risk difference	NNH	cOR (95% CI)	aOR (95% CI)
Cervical incompetence treated by cerclage	39 (0,2)	712 (0,1)	0,1	1000	4.60 (3.33-6.36)	4.58 (2.93-7.15)
Spontaneous preterm birth	781 (4,9)	57.019 (4,3)	0,6	167	1.15 (1.07-1.23)	1.11 (1.02-1.20)
SPTB < 32 weeks	150 (0,9)	7.788 (0,6)	0,3	333	1.61 (1.37-1.89)	1.52 (1.26-1.85)
SPTB < 28 weeks	85 (0,5)	3984 (0,3)	0,2	500	1.78 (1.43-2.21)	1.67 (1.30-2.15)
PIRP	571 (3,6)	35.822 (2,7)	0,9	111	1.35 (1.25-1.47)	1.32 (1.21-1.43)
Placenta praevia	41 (0,3)	1.315 (0,1)	0,2	500	2.62 (1.92-3.58)	2.48 (1.80-3.42)
Placental abruption	22 (0,1)	1.074 (0,1)	0	-	1.72 (1.13-2.62)	1.56 (1.02-2.39)
Retained placenta	512 (3,2)	33.521 (2,5)	0,7	142	1.30 (1.19-1.42)	1.26 (1.15-1.38)
Postpartum Haemorrhage	760 (5,0)	53.571 (4,1)	0,9	111	1.22 (1.14-1.32)	1.16 (1.08-1.25)
Any listed adverse outcome	1.750 (10,9)	124.586 (9,3)	1,6	63	1.20 (1.14-1.26)	1.15 (1.09-1.22)
Any listed adverse outcome other than cervical incompetence treated by cerclage	1.726 (10,8)	124.119 (9,2)	1,6	63	1.19 (1.13-1.25)	1.14 (1.08-1.21)

P-value for all outcomes < 0.001
 Spontaneous preterm birth (SPTB)= gestational age from 20 to 37 weeks, PIRP= placenta implantation or retention problems, NNH = number needed to harm, crude odds ratio (cOR) and adjusted odds ratio (aOR).
 aOR: OR are adjusted for known confounders for the given outcome. (SPTB) and cervical incompetence treated by cerclage are adjusted for maternal age, ethnicity, socioeconomic status (SES), parity, smoking, drug dependence, pyelitis, polyhydramnios, history of SPTB, history of cervical incompetence or Shirodkar procedure, history of uterine myoma and history of cervical surgery.
 aOR PIRP, placenta praevia, placental abruption and retained placenta are adjusted for maternal age, ethnicity, SES, parity, smoking, drug dependence, history of cesarean section and history of PIRP.
 aOR PPH is adjusted for maternal age, ethnicity, SES, parity, polyhydramnios, history of PPH, history of uterine myoma.
 aOR Composite outcome is adjusted for all the above mentioned.

Table 3. Gestational age at delivery in women with and without a history of pregnancy termination.				
Gestational age (weeks)	Termination of pregnancy in history (%)	Reference group (%)	cOR (95%CI)	aOR (95%CI)
20 ⁺⁰ - 23 ⁺⁶	43 (0,3)	1966 (0,1)	1.83 (1.35-2.48)	1.61 (1.13-2.30)
24 ⁺⁰ - 28 ⁺⁶	56 (0,4)	2658 (0,2)	1.76 (1.35-2.30)	1.67 (1.22-2.28)
29 ⁺⁰ - 32 ⁺⁶	80 (0,5)	5393 (0,4)	1.24 (0.99-1.55)	1.36 (1.07-1.74)
33 ⁺⁰ - 36 ⁺⁶	602 (3,8)	47.002 (3,5)	1.07 (0.99-1.16)	1.04 (0.95-1.14)
≥ 37	15.152 (95,1)	1.268.013 (95,7)	Reference group	Reference group
aOR are adjusted for maternal age, ethnicity, SES, parity, smoking, drug dependence, pyelitis, polyhydramnios, history of SPTB,, history of cervical incompetence or Shirodkarprocedure, history of uterine myoma, history of cervical sugery.				

For peer review only

Other Information

Funding:

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

No conflict of interest declaration:

"All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work."

Details of Contributors:

GCMLPC and AF initiated the study. BLS, GCMLPC, MPHK were involved in designing the study. BLS collected the data. BLS, MPHK, CWPMH analysed the data. All authors actively participated in interpreting the results and revising the paper, which was written by BLS, GCMLP, MPHK, AF and CWPMH.

Ethical approval: The board and privacy commission of the Netherlands Perinatal Registry approved this study.

Data sharing: Dataset is available on the Netherlands Perinatal Registry. Consent was not obtained, but presented data are anonymised.

Title page

The influence of pregnancy termination on the outcome of subsequent pregnancies: retrospective cohort study	Title
Brenda L Scholten, Godelieve C M L Page-Christiaens, Arie Franx, Chantal W P M Hukkelhoven, Maria P H Koster	Author's name
University Medical Center Utrecht, Lundlaan 6, 3584 EA, Utrecht, PO box 85090, 3508 AB, Utrecht, The Netherlands Brenda Scholten, MSc Department of Obstetrics, University Medical Center Utrecht, Godelieve Page-Christiaens, gynaecologist Department of Obstetrics, University Medical Center Utrecht, Arie Franx, professor of Obstetrics Netherlands Perinatal Registry, Mercatorlaan 1200, Room 46 PO box8588, 3503 RN, Utrecht, The Netherlands, Chantal Hukkelhoven, epidemiologist Department of Obstetrics, University Medical Center Utrecht, Maria Koster, epidemiologist	Address for each author
Godelieve Page-Christiaens, University Medical Center Utrecht, Lundlaan 6, Room KE 04.123.1, PO box 85090, 3508 AB Utrecht, The Netherlands, L.Christiaens@umcutrecht.nl Tel +31 88 755 6426, Fax +31 88 755 5320	Corresponding author
Termination of pregnancy, cervical incompetence, preterm delivery, placenta implantation and retention problems	Keywords
2.0534-870	Word count

Abstract

Objective: To compare the incidences of preterm delivery, cervical incompetence treated by cerclage, placenta implantation or retention problems (i.e. placenta praevia, placental abruption and retained placenta) and postpartum haemorrhage between women with and without a history of pregnancy termination.

Design: Retrospective cohort study using aggregated data from a national perinatal registry.

Setting: All midwifery practices and hospitals in the Netherlands.

Participants: All pregnant women with a singleton pregnancy without congenital malformations and a gestational age of ≥ 20 weeks who delivered between January 2000 and December 2007.

Main outcome measures: Preterm delivery, cervical incompetence treated by cerclage, placenta praevia, placental abruption, retained placenta and postpartum haemorrhage

Results: A previous pregnancy termination was reported in 16.000 (1.2%) deliveries. The vast majority of these (90-95%) were done by surgical methods. The incidence of all outcome measures was significantly higher in women with a history of pregnancy termination. Adjusted odds ratios (95% confidence interval) for cervical incompetence treated by cerclage, preterm delivery, placenta implantation or retention problems and postpartum haemorrhage were 4.6 (2.9-7.2), 1.11 (1.02-1.20), 1.42 (1.29-1.55) and 1.16 (1.08-1.25), respectively. Associated numbers needed to harm were 1000, 167, 111 and 111, respectively. For any listed adverse outcome the number needed to harm was 63.

Conclusions: In this large nationwide cohort study we found a positive association between surgical termination of pregnancy and subsequent was associated with an increased risk for preterm delivery, cervical incompetence treated by cerclage, placenta implantation or retention problems and postpartum haemorrhage in a subsequent pregnancy. Absolute risks for these outcomes however remain small. Medicinal termination might be considered first whenever there is a choice between both methods.

Article Summary

Article focus

- To estimate the influence of pregnancy termination on the outcome of subsequent pregnancies.
- Does termination of pregnancy lead to cervical incompetence and/or preterm delivery in subsequent pregnancies?
- Is termination of pregnancy associated with a higher risk of placenta implantation or retention problems (i.e. placenta praevia, placental abruption and retained placenta) in a subsequent pregnancy?

Key Messages

- Surgical A termination of pregnancy is positively associated with subsequent spontaneous an increased risk for preterm delivery, cervical incompetence treated by cerclage, placenta implantation/retention problems and postpartum hemorrhage in a subsequent singleton pregnancy.

Strengths and limitations of this study

- One of the ~~L~~ largest cohort studies on reproductive outcomes of women with and without a history of pregnancy termination.
- Registration of and adjustment for many potential confounders.
- The perinatal registry contains no information on the technique of pregnancy termination.
- The number of and gestational age at pregnancy terminations in a given woman was not registered
- Underreporting of pregnancy termination leads to an underestimation of its effect on future reproduction.

INTRODUCTION

Worldwide each year at least 43 million pregnancies are terminated, often in young nulliparous women.¹ Data on the effect on future pregnancies suggest an increase in risk for complications in subsequent pregnancies after pregnancy termination.²⁻¹³

In the Netherlands, approximately 32.000 pregnancies are terminated each year.¹⁴ The abortion rate has been unchanged since 2001 with 8.8 per thousand women of childbearing age (15 to 44 years) resident in the Netherlands having a pregnancy terminated each year.¹⁴ The vast majority (90-95%) of these abortions are performed in specialized clinics by surgical methods namely vacuum aspiration and curettage.¹⁴⁻¹⁵ In 1999, medicinal abortion with a combination of antiprogesteragens and prostaglandins has been introduced in clinical practice. However, in the Netherlands this method is mainly used for termination of pregnancy for medical or genetic reasons and usually not offered as an alternative to women requesting abortion for nonmedical reasons.

The question arises how women should be counseled as to the effect of surgical abortion on future reproductive performance. We therefore set out to compare the incidences of 1) preterm delivery, 2) cervical incompetence treated by cerclage, 3) placenta implantation or retention problems (PIRP) which include placenta praevia, placental abruption and retained placenta and 4) postpartum hemorrhage (PPH) in pregnancies of women with and without a history of pregnancy termination.

METHODS

Study population

Prospectively collected data were derived from the Netherlands Perinatal Registry (PRN).¹⁶ The PRN is a Dutch nationwide database that contains demographics and information about mother and newborn, course and outcome of pregnancy, and content and organization of care, all entered by health care providers. Around 96% of all deliveries from 20 weeks of gestation onwards are registered in the PRN. The database consists of three linked and validated registries: the national obstetric database for midwives (LVR-1), the national obstetric database for gynecologists (LVR-2) and the national neonatal/pediatric database (LNR).¹⁷⁻¹⁸ The study period was from January 2000 till and including December 2007. We chose this period to avoid byass, because medicinal termination of pregnancy was not commonly used at that time, the majority of pregnancy terminations being done surgically. All multiple births and births of a child with a congenital anomaly in index pregnancies were excluded. Also all women where labor was induced or a planned caesarean section was performed before 37 weeks gestation, i.e. iatrogenic preterm deliveries, were excluded (*Figure 1*). Whether there had been a previous termination of pregnancy or not was

registered based on responses given by the pregnant woman in a predefined pregnancy intake questionnaire, amongst others on reproductive history. In Dutch different terminology is used for pregnancy termination as opposed to miscarriage. This questionnaire is being filled out at the first prenatal visit, usually around 12 weeks of pregnancy. The number of pregnancy terminations in an individual woman is not registered in the PRN. The primary study outcomes were preterm delivery, cervical incompetence with placement of a cerclage, PIRP and PPH.

Definitions

Preterm delivery was registered from 20 weeks on and we therefore for this study defined preterm delivery as delivery between 20 and 37 weeks of gestation. The aim of the study was to document any registered possible adverse effects. For a subgroup analysis of gestational age at delivery we divided gestational age into 5 groups: 20⁺⁰ to 23⁺⁶ weeks, 24⁺⁰ to 28⁺⁶ weeks, 29⁺⁰ to 32⁺⁶ weeks, 33⁺⁰ to 36⁺⁶ weeks and 37 weeks and later. In the Netherlands a cervical cerclage is considered to be indicated when there is shortening or dilatation of the cervix without contractions during the second trimester of pregnancy.^{19,20} A history of pregnancy termination is not a reason for cerclage.

Placenta praevia, placental abruption and retained placenta have been merged into the composite measure PIRP because of the low incidence of these outcomes. Retained placenta also includes postpartum curettage for incomplete placenta. PPH was defined as more than 1000 milliliters estimated blood loss postpartum.

Prior cervical surgery includes conization or amputation of the cervix. Polyhydramnios was defined as an estimated amount of amniotic fluid of more than two liters, diagnosed by ultrasound during pregnancy.²¹ Perinatal mortality was defined as stillbirth or death up to 7 days after birth, after a gestation period of at least 22 weeks (WHO definition).

Socioeconomic status (SES) was based on the average income level of the neighborhood, which was determined by the first four digits of the woman's postal code, a common method for establishing SES in the Netherlands.

Statistical analysis

We used t-tests and chi-square tests to compare baseline characteristics and the difference in incidence of outcome measures between both groups. Logistic regression analysis was performed to calculate crude odds ratios (cOR) and adjusted odds ratios (aOR) and their 95% confidence intervals (95% CI). Odds ratios were adjusted for variables that are considered as possible confounders in the literature: maternal age, gravidity, parity, SES, ethnicity, smoking, drug dependence, pyelitis, polyhydramnios, current uterus myomatosis, history of preterm delivery, history of cervical incompetence, history of placenta praevia,

[history of](#) placental abruption, [history of](#) manual removal of the placenta, [history of](#) PPH (not due perineal trauma) and [history of](#) cervical surgery.²²⁻²⁷

A subgroup analysis of various categories of gestational age was performed for the outcome preterm delivery because a deleterious effect of cervical dilatation at time of delivery could be larger at early gestational ages.

We computed a number needed to harm (1/risk difference) in which the risk difference equaled the estimated incidence in women with a history of pregnancy termination minus the incidence among women without a history of pregnancy termination. All analyses were done using SPSS version 19. [Ethical approval was obtained from the board and privacy commission of the Netherlands Perinatal Registry.](#)

RESULTS

During the study period 1,357,894 singletons were born who fulfilled the selection criteria (*Figure 1*). In 16,000 deliveries (1.2%) the mother reported a history of pregnancy termination. Women with a history of pregnancy termination were more often younger than 20 or older than 35 years, were more often nulliparous, of non-Dutch origin, of lower socioeconomic status and more often smoked (*Table 1*). The incidences of preterm delivery, cervical incompetence treated by cerclage, PIRP and PPH are shown in *Table 2*. Cervical incompetence treated by cerclage was more frequently present in the group with a history of pregnancy termination (0.2% versus 0.1%; $p < 0.001$). Preterm delivery, PIRP and PPH were also more common in the group with a history of pregnancy termination (~~respectively 4.9% versus 4.3%; $p < 0.001$; 3.6% versus 2.7%; $p < 0.001$; 5.0% versus 4.1%; $p < 0.001$~~). All associations remained statistically significant after adjustment for possible confounders. The strongest association was found between cervical incompetence treated by cerclage and pregnancy termination with an aOR of 4.6 (95% CI 2.9-7.2). The aORs for preterm delivery, PIRP and PPH ~~are shown in *Table 2* were 1.11 (95% CI 1.02-1.20), 1.42 (95% CI 1.29-1.55) and 1.16 (95% CI 1.08-1.25), respectively.~~ Any listed adverse outcome occurred in 10.9% of the 16,000 deliveries with a history of pregnancy termination versus 9.3% in the reference group, aOR 1.15 (95% CI 1.09-1.22). The absolute risk difference for any listed adverse outcome amounted 1.6% with a number needed to harm of 63 women.

A subgroup analysis in gestational age at delivery categories showed that previous termination of pregnancy had the strongest association with preterm delivery at early gestational ages (*Table 3*). The strongest association was found for delivery between 20⁺⁰ and 23⁺⁶ weeks, cOR 1.83 (95% CI 1.35-2.48) and aOR 1.61 (95% CI 1.13-2.30).

DISCUSSION

The most important finding of this study was that termination of pregnancy is associated with an increased risk for preterm delivery, cervical incompetence, placenta implantation/retention problems and postpartum hemorrhage in a subsequent singleton pregnancy.

In the study period, 90-95% of pregnancy terminations were performed surgically.¹⁴⁻¹⁵ We therefore assume that the observed increased risks are related to surgical abortion. Cervical dilatation for terminating pregnancy can damage the cervix and cause cervical incompetence, leading to preterm delivery.²⁸ This risk is, amongst others, dependent on gestational age at termination and extent of dilatation. Placental implantation and retention problems are known to occur more often after uterine trauma such as previous caesarean delivery or uterine surgery.²⁹

A recent study in Scotland showed that surgical abortion was associated with a higher risk of preterm birth in a subsequent pregnancy than medicinal abortion.² The combined use of mifegyne and misoprostol is a safe medicinal alternative to surgical abortion but it is associated with a higher frequency of incomplete expulsion and longer post abortion bleeding.³⁰⁻³² Therefore, after 8 weeks of pregnancy it is mainly performed in a clinical setting. Studies on patient preferences show a high acceptability for both procedures, although the acceptability of medicinal abortion declines with increasing gestational age.^{31,33}

Strengths and weaknesses of this study

The major strengths of this study are the size of the cohort, the uniform coverage of almost all deliveries nationwide, the standardized history taking in all obstetric practices and the accurate documentation of history and pregnancy complications.

A limitation of this study is that a history of pregnancy termination is probably selectively reported (i.e. underreported) by pregnant women. The relatively low prevalence of pregnancy termination in the history in our database compared to the Dutch abortion registry and another (urban, high-risk) cohort study further marks this.^{34,35}

Presuming that women who did not report to have had a history of termination had the same risk of adverse outcome as those who did report this, underreporting has most likely weakened the associations in our study. As a result, this will have weakened the observed associations found in our study, and may thus have led to an underestimation of the effects. In other words, the increased risk of complications in subsequent pregnancies after (surgical) abortion are probably even higher. Secondly, some women have delivered more than once during the study period, and the sequence of various pregnancy outcomes is not known. Women may therefore have multiple records in the registry. These records cannot be linked to one another in the PRN data yet and therefore no adjustment could be made.

Another limitation is that curettage for spontaneous miscarriage is not registered in the PRN. This often does not require dilatation but the technique of uterine evacuation is the same.

These women are now undetected in the reference group, leading to an underestimation of the effect of ~~intrauterine manipulation pregnancy termination~~ on future reproduction.

Furthermore, neither gestational age at the moment of pregnancy termination nor number of terminations nor the technique of termination were available in the registry. In the Netherlands 58% of pregnancy terminations are performed before 8 weeks. In two thirds of the women registered in the (legally required) abortion registry it was the first termination, one quarter had had one previous termination and the remaining group had had 2 or more previous terminations.³⁴

Comparison with other studies

Previous literature suggested a small but definitive risk for adverse outcome in pregnancies following surgical abortion. ~~The large A recent systematic review of Lowit et al (3) reported an excess risk of preterm delivery of 5-12% (ORs 1.2-1.9) and an elevated risk of placenta praevia (ORs 1.3-1.7). More recently, a study of Bhattacharya et al (2) used similar methods as we did~~ and reported a higher risk of preterm birth and placental abruption in women with termination of pregnancy in their first pregnancy (n=67,745) versus women who had a live birth in their first pregnancy (n=357,080) (aOR 1.66 [95% CI 1.58-1.74] and 1.49 [95% CI 1.25-1.77] respectively). ~~More recently Klemitt et al (3) studied over 300.000 first time mothers from a 12 year period in the Medical Birth Register and linked their data to a 25 year period in the Finnish Abortion Registry. They found an association between preterm birth and previous abortion, with worse outcomes after multiple abortions. The abortion rate in Finland is similar to the one in the Netherlands.~~³⁴ A recent systematic review of Lowit et al (4) reported an excess risk of preterm delivery of 5-12% (ORs 1.2-1.9) and an elevated risk of placenta praevia (ORs 1.3-1.7). Another systematic review and meta-analysis of Shah et al (6) described a further increased risk for preterm delivery in women after two or more terminations of pregnancy (one termination in history OR 1.36 [95% CI 1.24-1.50] and two or more terminations OR 1.93 [95% CI 1.28-2.71]. Haldre et al (8) studied the occurrence of placenta complications in deliveries following an abortion and found a higher risk of retained placenta (aOR 1.23 [95% CI 1.1-1.38]). The range in ORs could be related to gestational age at the moment of termination. Termination of pregnancy at a lower gestational age requires less cervical dilatation and therefore the risk of cervical damage may be lower.

Implications of the study

Women who have had a termination of pregnancy have an increased risk of preterm delivery, cervical incompetence treated by cerclage, placental problems and postpartum hemorrhage although absolute risks are low. Medicinal termination may be safer for future pregnancies than surgical termination. For future research we recommend to include the technique of

pregnancy termination in perinatal registries, as well as gestational age at termination and number of terminations. The issue of possible harm to future reproduction is not routinely addressed when informing patients about various alternatives for terminating pregnancy. We recommend that this information should be included whenever there is a choice between both methods. The data generated in this study can be used for this purpose.

REFERENCES

1. Sedgh G, Singh S, Shah IH, Ahman E, Henshaw SK, Bankole A. Induced abortion: incidence and trends worldwide from 1995 to 2008. *Lancet* 2012;379:625-632.

2. Bhattacharya S, Lowit A, Bhattacharya S, Raja EA, Lee AJ, Mahmood T, et al. Reproductive outcomes following induced abortion: a national register-based cohort study in Scotland. *BMJ Open* 2012;2:e000911.doi:10.1136/bmjopen-2012-000911.

3. [Klemetti K, Gissler M, Niinimäki M, Hemminki E. Birth outcomes after induced abortion: a nationwide register-based study of births in Finland. *Hum Reprod* 2012; 27\(11\): 3315-20.](#)

4. Lowit A, Bhattacharya S, Bhattacharya S. Obstetric performance following an induced abortion. *Best Pract Res Clin Obstet Gynaecol* 2010;24:667-682.

5. Freak-Poli R, Chan A, Tucker G, Street J. Previous abortion and risk of pre-term birth: a population study. *J Matern Fetal Neonatal Med* 2009;22(1):1-7.

6. Voigt M, Henrich W, Zygmunt M, Frieze K, Straube S, Briesse V. Is induced abortion a risk factor in subsequent pregnancy? *J Perinat. Med.* 2009;37:144-149.

7. Shah PS, Zao J. Induced termination of pregnancy and low birth weight and preterm birth: a systematic review and meta-analyses. *BJOG* 2009;116:1425-42.

8. Brown JS, Adera T, Masho SW. Previous abortion and the risk of low birth weight and preterm births. *J epidemiol Community Health* 2008;62:16-22.

9. Haldre K, Rahu K, Karro H, Rahu M. Previous history of surgically induced abortion and complications of the third stage of labour in subsequent normal vaginal deliveries. *J Matern Fetal Neonatal Med* 2008;21(12):884-888.

10. Reime B, Schücking BA, Wenzlaff P. Reproductive outcomes in adolescents who had a previous birth or an induced abortion compared to adolescents' first pregnancies. *BMC Pregnancy Childbirth* 2008; 8:4.

11. Chasen ST, Kalish RB, Gupta M, Kaufman J, Chervenak FA. Obstetric outcomes after surgical abortion at ≥ 20 weeks' gestation. *Am J Obstet Gynecol* 2005;193:1161-4.

12. Ancel PY, Lelong N, Papiernik E, Saurel-Cubizolles MJ, Kaminski M. History of induced abortion as a risk factor for preterm birth in European countries: results from the EUROPOP survey. *Hum Reprod* 2004;19:734-40.

13. Moreau C, Kaminski M, Ancel PY, Bouyer J, Escande B, Thiriez G. Previous induced abortions and the risk of very preterm delivery: results of the EPIPAGE study. *BJOG* 2005;112:430-7.
14. Lee L, Wijzen C. Annual report Abortion Registration 2006. Utrecht: Rutgers NissoGroep; 2007. Available from: http://www.rutgerswpf.nl/sites/default/files/rapport_LAR_2006.pdf
15. Lee L, Wijzen C. Annual report Abortion Registration 2007. Utrecht: Rutgers NissoGroep; 2008. (With a summary in English on page 7.) Available from: http://www.rutgerswpf.nl/sites/default/files/rapport_LAR_2007.pdf
16. Perinatreg.nl [internet]. Utrecht: The Netherlands Perinatal Registry. Available from: http://www.perinatreg.nl/home_english
17. Méray N, Reitsma JB, Ravelli AC, Bonse GJ. Probabilistic record linkage is a valid and transparent tool to combine databases without a patient identification number. *J Clin Epidemiol*. 2007;60:883-91
18. Tromp M, Ravelli AC, Meray N, Reitsma JB, Bonse GJ. An efficient validation method of probabilistic record linkage including readmissions and twins. *Methods Inf Med*. 2008;47:356-63
19. NVOG Richtlijn "Preventie recidief spontane vroeggeboorte" 2007. (Guideline Dutch Society of Obstetrics and Gynaecology: prevention relapse spontaneous preterm birth, March 2007). 2007. Utrecht. Available at: http://nvog-documenten.nl/index.php?pagina=/richtlijn/item/pagina.php&richtlijn_id=745. Accessed Jan 23, 2013.
20. Althuisius SM, Dekker GA, Geijn HP, Bekedam DJ, Hummel P. Cervical incompetence prevention randomized cerclage trial: study (CIPRACT). *Am J Obstet Gynecol* 2001;185:1107-1112.
21. Croom CS, Banias BB, Ramos-Santos E, Devoe LD, Bezhadian A, Hiatt AK. Do semiquantitative amniotic fluid indexes reflect actual volume? *Am J Obstet Gynecol*. 1992 Oct;167(4 Pt 1):995-9
22. Kwee A, Bots ML, Visser GHA, Bruinse HW. Emergency peripartum hysterectomy: A prospective study in the Netherlands. *Eur J Obstet Gynecol Reprod Biol* 2006;124:187-92.
23. Goldenberg R, Culhane JF, Lams JD, Romero R. Epidemiology and causes of preterm birth. *Lancet* 2008; 371:75-84.
24. Raatikainen K, Heiskanen N, Heinonen S. Induced abortion: not an independent risk factor for pregnancy outcome, but a challenge for health counseling. *Ann Epidemiol* 2006;16:587-92.
25. Sheiner E, Sarid L, Levy A, Seidman DS, Hallak M. Obstetric risk factors and outcome of pregnancies complicated with early postpartum haemorrhage: a population-based study. *J Matern Fetal Neonatal Med* 2005; 18:149-154.

26. Iyasu S, Saftlas AK, Rowley DL, Koonin LM, Lawson HW, Atrash HK. The epidemiology of placenta previa in the United States, 1979 through 1987. *Am J Obstet Gynecol*. May 1993;68(5):1424-9.

27. [Schaaf JM, Ravelli CJ, Mol BWJ, Abu-Hanna A. Development of a prognostic model for predicting spontaneous singleton preterm birth. *Eur J Obstet Gynecol Reprod Biol* 2012; 164:150-155.](#)

28. Whitley KA, Trinchere K, Prutsman W, et al. Midtrimester dilation and evacuation versus prostaglandin induction: a comparison of composite outcomes. *Am J Obstet Gynecol* 2011;205:386.

29. Kwee A, Bots ML, Visser GHA, Bruinse HW. Obstetric management and outcome of pregnancy in women with a history of caesarean section in the Netherlands. *Eur J Obstet Gynecol Reprod Biol*. 2007;132:171-76.

30. Say L, Brahma D, Kulier R, Campana A, Guimezoglu AM. Medical versus surgical methods for first trimester termination of pregnancy. *Cochrane Database of Systematic Reviews* 2002, Issue 4. Art. No.: CD003037. DOI: 10.1002/14651858.CD003037.pub2

31. Robson SC, Kelly T, Howel D, Deverill M, Hewison J, Lie MLS, Stamp E, Armstrong N, May CR. Randomised preference trial of medical versus surgical termination of pregnancy less than 14 weeks' gestation (TOPS). *Health Technol Assess* 2009;13(53).

32. Graziosi GCM, Mol BWJ, Reuwer PJH, Drogtop A, Bruinse HW. Misoprostol versus curettage in women with early pregnancy failure after initial expectant management: a randomized trial. *Hum Reprod* 2004;19(8):1894-9.

33. Rørbye C, Nørgaard M, Nilas L. Medical versus surgical abortion: comparing satisfaction and potential confounders in a partly randomized study. *Hum. Reprod*. 2005;20:834–838.

34. The Health Care Inspectorate. Annual report 2009 Termination of Pregnancy Act. The Hague; 2010 (with a summary in English on page 29).

35. Vrijkotte T.G.M. (2012). Amsterdam Born Children and their Development (ABCD Study). Unpublished raw data.

Figure 1. Patient selection

Preterm delivery: delivery at a gestational age ~~between~~~~from~~ 20 ~~and~~~~to~~ 37 weeks. CI treated by cerclage: cervical incompetence treated by cerclage. PIRP (placenta implantation and retention problems): placenta praevia, placental abruption or retained placenta.

Table 1. Patient characteristics		
Characteristics	Termination of pregnancy in history (%)	Reference group (%)
Study population	16.000	1.341.894
Maternal age^a		
Mean (SD)	30,41 (5,8762)	30,40 (4,839)
<20	525 (3,3)	22.786 (1,7)
20 – 25	2.983 (18,6)	187.355 (14)
26 – 30	4.085 (25,5)	447.307 (33,3)
31 – 35	5.186 (32,4)	495.546 (36,9)
> 35	3.219 (20,1)	188.591 (14,1)
Parity^a		
0	9.265 (57,9)	613.755 (45,7)
1	4.692 (29,3)	485.287 (36,2)
2	1.453 (9,1)	169.802 (12,7)
3	417 (2,6)	46.910 (3,5)
≥ 4	172 (1,1)	25.822 (1,9)
SES^{a,b}		
High	3.469 (21,7)	314.667 (23,4)
Normal	5.488 (34,3)	608.113 (45,3)
Low	6.861 (43,0)	402.254 (30,0)
Ethnicity^a		
Dutch	10.304 (64,4)	1.093.438 (81,5)
Mediterranean	1.184 (7,4)	105.368 (7,9)
Other European	1.012 (6,3)	33.728 (2,5)
Creole	1.441 (9,0)	30.226 (2,3)
Hindu	341 (2,1)	14.523 (1,1)
Asian	605 (3,8)	24.408 (1,8)
Other	1.086 (6,8)	31.519 (2,3)
Smoking ^a	180 (1,1)	5.712 (0,4)
Drug dependence ^a	91 (0,6)	1.232 (0,09)
Reproductive history		
Preterm delivery ^a	165 (1,0)	16.122 (1,2)
Cervical incompetence/ Shirodkarprocedure	3 (0,02)	381 (0,03)
Placenta praevia ^a	8 (0,05)	183 (0,01)
Placental abruption	17 (0,1)	2023 (0,2)
Manual removal of the placenta	75 (0,5)	7.353 (0,5)
Postpartum Haemorrhage ^a	156 (1,0)	19.062 (1,4)
Cesarean section ^a	839 (5,2)	101.884 (7,6)
Cervical surgery ^a	28 (0,2)	1.424 (0,1)
Uterine myoma ^a	79 (0,5)	4.732 (0,4)
Myomectomy subserous	5 (0,03)	257 (0,02)
Myomectomy submucous/intramural	4 (0,03)	409 (0,03)
Index gravidity		
Pyelitis ^a	20 (0,1)	736 (0,05)
Polyhydramnios	5 (0,03)	234 (0,02)
Mode of delivery^a		
Spontaneous vaginal delivery	12.048 (75,4)	1.024.044 (76,4)
Instrumental vaginal delivery	1.682 (10,5)	143.654 (10,7)
Elective caesarean delivery	738 (4,6)	70.345 (5,2)
Emergency caesarean delivery	1.520 (9,5)	102.090 (7,6)
Perinatal mortality ^a	109 (0,7)	7602 (0,6)
^a P value < 0.05, ^b socioeconomic status (SES)		

Table 2. Pregnancy outcomes in patients with and without a history of pregnancy termination.

Outcome	Termination of pregnancy in history (%)	Reference group (%)	Risk difference	NNH	cOR (95% CI)	aOR (95% CI)
Cervical incompetence treated by cerclage	39 (0,2)	712 (0,1)	0,1	1000	4.60 (3.33-6.36)	4.58 (2.93-7.15)
Spontaneous preterm birth	781 (4,9)	57.019 (4,3)	0,6	167	1.15 (1.07-1.23)	1.11 (1.02-1.20)
SPTB < 32 weeks	150 (0,9)	7.788 (0,6)	0,3	333	1.61 (1.37-1.89)	1.52 (1.26-1.85)
SPTB < 28 weeks	85 (0,5)	3984 (0,3)	0,2	500	1.78 (1.43-2.21)	1.67 (1.30-2.15)
PIRP	571 (3,6)	35.822 (2,7)	0,9	111	1.35 (1.25-1.47)	1.32 (1.21-1.43)
Placenta praevia	41 (0,3)	1.315 (0,1)	0,2	500	2.62 (1.92-3.58)	2.48 (1.80-3.42)
Placental abruption	22 (0,1)	1.074 (0,1)	0	-	1.72 (1.13-2.62)	1.56 (1.02-2.39)
Retained placenta	512 (3,2)	33.521 (2,5)	0,7	142	1.30 (1.19-1.42)	1.26 (1.15-1.38)
Postpartum Haemorrhage	760 (5,0)	53.571 (4,1)	0,9	111	1.22 (1.14-1.32)	1.16 (1.08-1.25)
Any listed adverse outcome	1.750 (10,9)	124.586 (9,3)	1,6	63	1.20 (1.14-1.26)	1.15 (1.09-1.22)
Any listed adverse outcome other than cervical incompetence treated by cerclage	1.726 (10,8)	124.119 (9,2)	1,6	63	1.19 (1.13-1.25)	1.14 (1.08-1.21)

P-value for all outcomes < 0.001

Spontaneous preterm birth (SPTB)= gestational age from 20 to 37 weeks, PIRP= placenta implantation or retention problems, NNH = number needed to harm, crude odds ratio (cOR) and adjusted odds ratio (aOR).

aOR: OR are adjusted for known confounders for the given outcome. (SPTB)PB and cervical incompetence treated by cerclage are adjusted for maternal age, ethnicity, socioeconomic status (SES), parity, smoking, drug dependence, pyelitis, polyhydramnios, and in history of SPTB, history of cervical incompetence and/or Shirodkar procedure, history of uterine myoma and history of cervical surgery.

aOR PIRP, placenta praevia, placental abruption and retained placenta are adjusted for maternal age, ethnicity, SES, parity, smoking, drug dependence, and in history of cesarean section and history of PIRP.

aOR PPH is adjusted for maternal age, ethnicity, SES, parity, polyhydramnios, and in history of PPH, history of and uterine myoma.

aOR Composite outcome is adjusted for all the above mentioned.

Table 3. Gestational age at delivery in women with and without a history of pregnancy termination.				
Gestational age (weeks)	Termination of pregnancy in history (%)	Reference group (%)	cOR (95%CI)	aOR (95%CI)
20 ⁺⁰ - 23 ⁺⁶	43 (0,3)	1966 (0,1)	1.83 (1.35-2.48)	1.61 (1.13-2.30)
24 ⁺⁰ - 28 ⁺⁶	56 (0,4)	2658 (0,2)	1.76 (1.35-2.30)	1.67 (1.22-2.28)
29 ⁺⁰ - 32 ⁺⁶	80 (0,5)	5393 (0,4)	1.24 (0.99-1.55)	1.36 (1.07-1.74)
33 ⁺⁰ - 36 ⁺⁶	602 (3,8)	47.002 (3,5)	1.07 (0.99-1.16)	1.04 (0.95-1.14)
≥ 37	15.152 (95,1)	1.268.013 (95,7)	Reference group	Reference group
aOR are adjusted for maternal age, ethnicity, SES, parity, smoking, drug dependence, pyelitis, polyhydramnios, uterine myoma, cervical surgery and in history of SPTB, preterm birth , history of cervical incompetence and/or Shirodkarprocedure, history of uterine myoma, history of cervical sugery .				

Other Information

Funding:

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

No conflict of interest declaration:

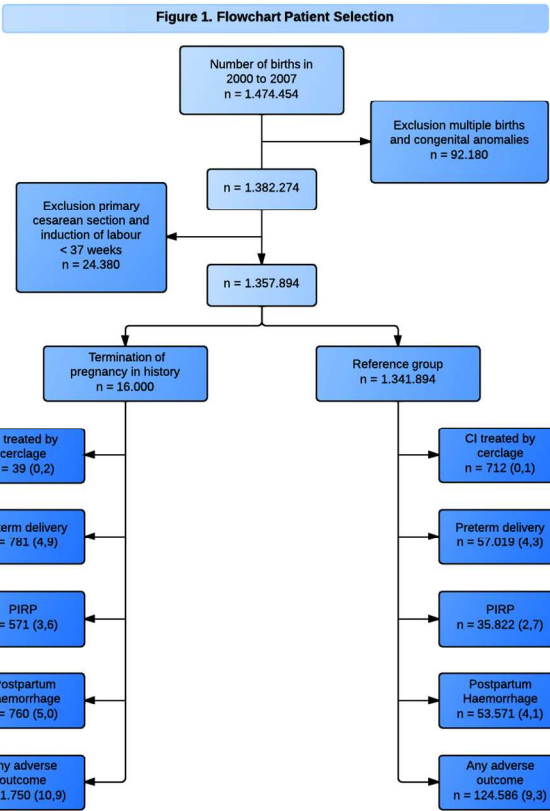
"All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work."

Details of Contributors:

GCMLPC and AF initiated the study. BLS, GCMLPC, MPHK were involved in designing the study. BLS collected the data. BLS, MPHK, CWPMH analysed the data. All authors actively participated in interpreting the results and revising the paper, which was written by BLS, GCMLP, MPHK, AF and CWPMH.

Ethical approval: The board and privacy commission of the Netherlands Perinatal Registry approved this study.

Data sharing: Dataset is available on the Netherlands Perinatal Registry. Consent was not obtained, but presented data are anonymised.



Preterm delivery: gestation age from 20 to 37 weeks. CI treated by cerclage: cervical incompetence treated by cerclage. PIRP (placenta implantation and retention problems): placenta praevia, placental abruption or retained placenta.

479x620mm (72 x 72 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	1
		(b) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4,5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	4,5
		(b) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4,5
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	5
		(b) Describe any methods used to examine subgroups and interactions	5
		(c) Explain how missing data were addressed	N/A
		(d) If applicable, explain how loss to follow-up was addressed	N/A
		(e) Describe any sensitivity analyses	5
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) Summarise follow-up time (eg, average and total amount)	4,5
Outcome data	15*	Report numbers of outcome events or summary measures over time	6
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 2
		(b) Report category boundaries when continuous variables were categorized	6
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	6
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6, table 3
Discussion			
Key results	18	Summarise key results with reference to study objectives	6
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8
Generalisability	21	Discuss the generalisability (external validity) of the study results	7,8
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	N/A

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at <http://www.plosmedicine.org/>, Annals of Internal Medicine at <http://www.annals.org/>, and Epidemiology at <http://www.epidem.com/>). Information on the STROBE Initiative is available at www.strobe-statement.org.